

Coronary artery surgery in women compared with men: analysis of coronary risk factors and in-hospital mortality in a single centre

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Abstract

Objective—To determine differences in coronary risk factors between women and men and their relation to in-hospital mortality associated with coronary artery bypass grafting.

Design—Prospective observational study.

Setting—A regional cardiothoracic centre.

Patients—482 (362 (75%) men and 120 (25%) women) consecutive patients who had primary isolated coronary artery bypass grafting.

Results—The women were on average three years older than the men (63 v 60 years, $P < 0.001$). Women more frequently had hypertension (47% v 33%, $P < 0.01$), diabetes mellitus (21% v 10%, $P < 0.005$), hypothyroidism (9% v 2%, $P < 0.003$), and a family history of premature coronary heart disease (49% v 31%, $P < 0.0006$). More of the men were cigarette smokers (67% v 45%, $P > 0.00001$). Many of the women and men had dyslipidaemia. Postmenopausal women had a higher concentration of serum total cholesterol than men of a comparable age, (7.3 mmol/l v 6.5 mmol/l, $P = 0.0002$). Although arterial grafts were often used in both sexes, they were more often used in men than in women (91% v 78% respectively, $P = 0.0003$). In-hospital mortality was 2.1% (1.4% in men and 4.2% in women, $P = 0.14$). The estimated one year probability of survival in men who had survived 30 days was 0.99 with 95% confidence interval 0.98 to approximately 1 while that for women was 0.97 with 95% confidence interval 0.91 to approximately 1. Univariate analysis showed that preoperative history of diabetes mellitus was a predictor of mortality ($P = 0.03$).

Conclusion—There were differences in the incidence and type of risk factors in men and women who had coronary artery bypass grafting. Preoperative diabetes mellitus was a predictor of in-hospital mortality.

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In the United Kingdom coronary heart disease is the leading cause of death in women over 65 years of age and a major contributor to mortality in younger women.¹ Whereas the disease is less prevalent in premenopausal women than in men, its incidence increases

rapidly after the menopause so that rates of coronary disease are almost equal in women and men over sixty.²

In 1991 in England and Wales 68 479 women and 81 611 men died of coronary heart disease.¹ The latest data available from the World Health Organisation show that mortality from coronary heart disease in women is highest in Scotland (121/100 000) where it is almost double that in the United States (67/100 000).³

At all ages the incidence of coronary artery disease in women has increased and its outcome seems worse than that in men suggesting a different type of disease⁴ and possibly a different set of risk factors. Most studies showed that the immediate and long-term prognosis in women is worse than that in men after myocardial infarction⁵⁻⁷ and after therapeutic interventions such as coronary balloon angioplasty.⁸ Coronary artery bypass grafting (CABG) remains the most commonly used form of myocardial revascularisation, however, there is perceived to be a possible bias against women in terms of the application of coronary angiography and CABG. This has been the subject of extensive debate.⁹ Coronary surgery is thought to carry higher operative mortality in women than in men.¹⁰⁻¹⁷ This excess in mortality has been attributed to several factors including age, functional class, a smaller body,¹⁸ severity of coronary heart disease (CHD), and the technical difficulties of operating on women.^{12,13} The relative incidence of coronary risk factors in women and men undergoing CABG and the possible influence on early mortality has not been adequately studied.

We have studied the differences in risk factors between men and women and their relation to hospital mortality associated with CABG.

Patients and methods

From 1 January 1991 to 31 May 1993 all patients admitted under one of two surgical teams at Harefield Hospital for primary CABG were included in the study. We did not include patients undergoing CABG incidental to heart valve replacement or repair, resection of ventricular aneurysm, or other surgical procedures. We studied 482 consecutive patients (362 (75%) men and 120 (25%) women). To compare men and women we collected data on patient age; body mass index; body surface area; hypertension, diabetes mellitus, and hypothyroidism requiring

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therapy; peripheral vascular disease; previous myocardial infarction; family history of premature coronary artery disease; cigarette smoking; preoperative medications; preoperative fasting lipids and lipoproteins; type of graft (venous or arterial), and state at hospital discharge (alive or dead) and follow up. In-hospital mortality was defined as death occurring within 30 days of CABG.

Preoperative fasting serum, total cholesterol, and triglyceride were analysed enzymatically, as was high density lipoprotein cholesterol after precipitation with heparin-manganese. The concentration of low density lipoprotein (LDL) cholesterol was calculated by the formula of Friedewald *et al*¹⁹ except in patients with triglyceride concentrations 4.5 mmol/l in whom LDL cholesterol was measured after ultracentrifugation of serum.²⁰ Body surface area was calculated by the method of Dubois and Dubois²¹:

$$\sqrt{\frac{\text{height (cm)} \times \text{weight (kg)}}{3600}}$$

STATISTICAL ANALYSIS

We used the two sample *t* test for independent variables and the χ^2 test with Yates' correction as appropriate to compare differences

between groups. It is generally accepted that the average age of menopause is 51.4 years with a gaussian distribution ranging from 40 to 58 years.²² We compared men and women with and without stratification by age (below 51.4 years premenopausal and above 51.4 years postmenopausal) because not all women aged < 51.4 years are premenopausal and not all those aged > 51.4 years are postmenopausal.

The confidence intervals for the probability of survival were obtained from the observed proportions of male and female patients surviving to 30 days after operation. In view of the low mortality, it was appropriate to evaluate these directly from the underlying binomial distribution rather than to use a normal approximation and quote standard errors.²³

Triglyceride values were log transformed (because of skewed distribution) before statistical analysis (table 3 shows untransformed values). In all analyses a difference of *P* < 0.05 was regarded as statistically significant.

Results

Table 1 shows the prevalence of coronary risk factors. On average women were 3 years older than men (63 *v* 60 years, *P* < 0.001) and the mean body mass index was slightly higher. Women more likely to have hypertension (47% *v* 33%, *P* < 0.01), diabetes mellitus (21% *v* 10%, *P* < 0.005), hypothyroidism (9% *v* 2%, *P* < 0.0003), and a family history of premature coronary heart diseases (49% *v* 31%, *P* < 0.0006).

The incidence of preoperative myocardial infarction was high in women (53%) and men (55%) and similar percentages of women (9%) and men (7%) had peripheral vascular disease.

Though a similar proportion of women

Table 1 Comparison of risk factors in women and men undergoing coronary artery bypass grafting (mean (SE) and percentages as appropriate)

Variable and group	Women (n = 120) (< 51.4yr = 11 > 51.4yr = 109)	Men (n = 362) (< 51.4yr = 56 > 51.4yr = 306)	P
Age (yr):			
All	63 (0.7)	60 (0.5)	0.001
< 51.4yr	48 (0.6)	45 (0.6)	0.0008
> 51.4yr	64 (0.6)	63 (0.4)	0.05
Body surface area (m ²):			
All	1.75 (0.01)	1.95 (0.008)	0.0001
< 51.4yr	1.82 (0.08)	1.96 (0.025)	NS
> 51.4yr	1.75 (0.015)	1.95 (0.006)	0.0001
Body mass index (kg/m ²):			
All	26.69 (0.39)	26.33 (0.17)	NS
< 51.4yr	27.16 (2.0)	26.37 (0.50)	NS
> 51.4yr	26.64 (0.40)	26.33 (0.17)	NS
Hypertension (requiring therapy) (%):			
All	47	33	0.01
< 51.4yr	20	27	NS
> 51.4yr	50	35	0.009
Diabetes mellitus (requiring therapy) (%):			
All	21	10	0.0005
< 51.4yr	11	11	NS
> 51.4yr	22	10	0.004
Hypothyroidism (requiring therapy) (%):			
All	9	2	0.0003
< 51.4yr	22	0	0.01
> 51.4yr	8	2	0.007
Peripheral vascular disease (%):			
All	9	7	NS
< 51.4yr	0	5	NS
> 51.4yr	10	7	NS
Previous MI (%):			
All	53	55	NS
< 51.4yr	80	59	NS
> 51.4yr	50	54	NS
Family history of heart disease (%):			
All	49	31	0.0006
< 51.4yr	40	50	NS
> 51.4yr	50	27	0.0001
Cigarette smoking (%):			
All	45	67	0.00001
< 51.4yr	60	70	NS
> 51.4yr	44	66	0.00001

BMI, body mass index; CHD, coronary heart disease; MI, myocardial infarction. Smokers were currently smoking > 10 cigarettes/day or had given up less than a year before.

Table 2 Comparison of preoperative class of medication in women and men (results all expressed as percentages)

Variables and Group	Women (n = 120) (< 51.4yr = 11 > 51.4yr = 109)	Men (n = 362) (< 51.4yr = 56 > 51.4yr = 306)	P
β blockers:			
All	58	59	NS
< 51.4yr	50	59	NS
> 51.4yr	59	60	NS
Diuretics:			
All	34	16	0.0001
< 51.4yr	30	14	NS
> 51.4yr	35	16	0.0001
Lipid lowering drugs:			
All	17	7	0.002
< 51.4yr	20	11	NS
> 51.4yr	17	6	0.002
ACE inhibitors:			
All	11	8	NS
< 51.4yr	20	7	NS
> 51.4yr	10	9	NS
Calcium antagonist:			
All	52	49	NS
< 51.4yr	50	47	NS
> 51.4yr	57	51	NS
Oral nitrates:			
All	78	82	NS
< 51.4yr	90	77	NS
> 51.4yr	77	83	NS

Table 3 Preoperative fasting serum lipids and lipoproteins value (mean (SE))

Variable and group	Women (n = 120) (< 51.4 yr = 11 > 51.5 yr = 109)	Men (n = 362) (< 51.4 yr = 56 > 51.4 yr = 306)	P
Total cholesterol (mmol/l):			
All	7.3(0.1)	6.5(0.1)	0.0002
< 51.4 yr	6.7(0.4)	6.5(0.2)	NS
> 51.4 yr	7.3(0.1)	6.5(0.1)	0.0002
Triglyceride (mmol/l):			
All	2.7(0.22)	2.5(0.18)	NS
< 51.4 yr	2.1(0.23)	2.2(0.29)	NS
> 51.4 yr	2.7(0.24)	2.5(0.21)	NS
HDL cholesterol (mmol/l):			
All	1.1(0.04)	1.1(0.03)	NS
< 51.4 yr	1.1(0.12)	1.1(0.04)	NS
> 51.4 yr	1.1(0.04)	1.1(0.04)	NS
LDL cholesterol (mmol/l):			
All	4.8(0.2)	4.6(0.08)	NS
< 51.4 yr	4.5(0.6)	4.6(0.15)	NS
> 51.4 yr	4.8(0.17)	4.6(0.09)	NS

Table 4 Comparison of venous and arterial grafts in women and men (mean (SE))

Variable and group	Women (n = 120) (< 51.4 yr = 11 > 51.4 yr = 109)	Men (n = 362) (< 51.4 yr = 56 > 51.4 yr = 306)	P
Number of venous grafts:			
All	2.4(0.08)	2.5(0.04)	NS
< 51.4 yr	2.4(0.15)	2.1(0.13)	NS
> 51.4 yr	2.5(0.1)	2.5(0.05)	NS
Number of arterial grafts:			
All	0.8(0.04)	1.0(0.03)	0.0003
< 51.4 yr	0.8(0.12)	1.14(0.06)	0.032
> 51.4 yr	0.8(0.05)	0.93(0.03)	0.002

(60%) and men (70%) below the age of 51.4 years were cigarette smokers; men aged > 51.4 years were more likely than women of the same age to be cigarette smokers (66% *v* 44%, $P < 0.00001$).

Table 2 shows preoperative medications in women and men. Women were more likely to be taking diuretics (34% *v* 16%, $P = 0.0001$) and lipid lowering drugs (17% *v* 6%, $P = 0.0002$) than men of the same age; however, there was no difference in proportion of women and men on β blockers, ACE inhibitors, calcium antagonists, and oral

nitrates. Women over 51.4 years (postmenopausal) had a higher concentration of serum total cholesterol than men of a similar age (table 3) (7.3 mmol/l *v* 6.5 mmol/l, $P = 0.0002$). There was no significant difference in serum triglycerides, HDL cholesterol, and LDL cholesterol (table 3).

Though most women and men in this study received arterial grafts, men were more likely to receive an arterial graft (78% *v* 91%, $P = 0.0003$). Overall those receiving arterial grafts were younger (60.1 years *v* 64.9 years, $P = 0.00001$) (59.4 years *v* 65.8 years, $P = 0.00001$ in men and 62.6 years *v* 63.7 years, $P = 0.48$, in women). Fewer patients with diabetes mellitus (77%) received arterial grafts than those without (87%) ($P = 0.044$). Comparable figures in women were 62.5% and 79.8% ($P = 0.048$) and in men they were 86.5% and 88.7% ($P > 0.1$). Table 4 compares the use of arterial and venous grafts in women and men.

OPERATIVE MORTALITY

There were 10 (2.1%) early deaths (within 30 days of CABG). Mortality for men was 1.4% (5/362) and for women 4.2% (5/120) ($P = 0.14$). Table 5 shows detailed characteristics of the 10 patients who died: these patients had severe three vessel disease, in addition 70% had unstable angina and 50% were admitted for emergency surgery. There were three late deaths: two women and one man died during the follow up of 1 year. The estimated probability of survival for 30 days in men was 0.99 (95% CI 0.97 to 0.99) while that for women was 0.96 (95% CI 0.90 to 0.99).

The estimated 1 year probability of survival for men who survived 30 days was 0.99 (95% CI 0.98 to approximately 1) while that for women was 0.97 (95% CI 0.91 to approximately 1).

In univariate analysis a preoperative history of diabetes mellitus was found to be a significant predictor of in-hospital mortality ($p = 0.03$). None of the other variables including age, sex, body surface area, and hypertension showed statistically significant effects on mortality.

Discussion

Differences between men and women in potential risk factors for severe coronary artery disease requiring CABG were identified in this study. Women were significantly older than men and more frequently had hypertension, diabetes mellitus, hypercholesterolaemia, hypothyroidism, and a family history of premature coronary artery disease. Studies suggest that hypertension is a major risk factor for coronary heart disease in women.^{24 25} We found that hypertension was more prevalent among postmenopausal women than among men of the same age. Staessen *et al* reported a fourfold higher prevalence of hypertension in postmenopausal women than in premenopausal women (40% *v* 10%, $P < 0.001$).²⁶ The reason for this difference remains unexplained. Prospective studies confirmed that

Table 5 Data on operative deaths

Case No	Sex	Age (yr)	V Preop state	Vessels diseased (n)	LVEF	Cause of death	Time of death	Priority of surgery
1	F	53	PI,UA	3	45	AMI	5 days	Emergency
2	F	72	UA	3 + LM	50	PE	12 days	Emergency
3	F	51	PI,UA	3	45	HF	1 day	Emergency
4	F	65	UA,COPD	3	45	HF	Same day	Elective
5	F	61	SA,	3	40	HF	ITU Same day	Elective
6	M	69	PI,UA	3	20	HF	1 day	Emergency
7	M	63	PI,UA	3	18	HF	22 days	Emergency
8	M	58	SA,	3	50	HF	2 days	Elective
9	M	67	SA,	3	40	HF	15 days	Elective
10	M	72	PI,UA	3	20	HF + RF	3 days	Elective

AMI, acute myocardial infarction; COPD, chronic obstructive pulmonary disease; HF, heart failure; PI, postmyocardial infarction; PE, pulmonary embolism; RF, renal failure; SA, stable angina; UA, unstable angina; LM, left main stem.

diabetes mellitus is an independent risk factor for coronary heart disease in women.^{27, 28} Our study and that of Kennel and McGee suggest that the attributable risk of diabetes for coronary artery disease is higher in women than in men.²⁷ In addition, we found that diabetes mellitus is a predictor of in-hospital mortality after CABG. Similar findings were reported by Fietsam *et al.*²⁹ The importance of diabetes as a risk factor may be related to the accompanying atherosclerosis and impairment of the autonomic nervous system. Autonomic dysfunction and neuropathy in diabetic patients cause a high incidence of silent myocardial infarction and have a considerable impact on changes in blood pressure and heart rate during anaesthesia.^{30, 31} Diabetic patients also require more intraoperative vasopressors and inotropes to support the circulation³⁰ and have a high risk of respiratory failure and arrhythmias after CABG.²⁹ Identification and appropriate management of these complications could reduce the risk in this subset of patients.

In this study a high proportion of women and men had raised concentrations of fasting serum total cholesterol, triglycerides, and LDL cholesterol. Although more women were treated with lipid lowering drugs, their total fasting serum cholesterol was significantly higher than that of men. Several epidemiological studies confirm that raised concentrations of cholesterol are a risk factor for coronary artery disease in women.^{24, 31, 32} Data from the Framingham Study demonstrate a direct relation between total cholesterol concentration and annual rate of coronary artery disease.³² Women with a total cholesterol concentration above 6.85 mmol/l had an approximately twofold higher risk of coronary artery disease than women with a cholesterol concentration of ≤ 5.3 mmol/l. Other studies suggest that triglyceride concentrations are also an important risk factor in women.^{33, 34}

Though most secondary prevention trials of regression of coronary artery disease have included few women the studies of Ornish *et al.*³⁵ and Kane *et al.*³⁶ suggest that the anticipated benefit of lipid lowering drugs with diet in the treatment of atherosclerosis applies to women as well as to men and, they suggest that the ability to undergo coronary atherosclerotic regression is greater in women.

We found no difference in in-hospital mortality in women and men below the age of 51.4 years (0%). Mortality in women above the age of 51.4% (postmenopausal) was 4.2% and in men it was 1.4% ($P = 0.14$). The mortality in women resembled that reported by Khan *et al.* (4.6%) and O'Connor *et al.* (7.1%).^{15, 37}

Our data did not show any significant effect of body surface area, body mass index, or age on in-hospital mortality. Loop *et al.*, however, suggested that body surface area was the strongest predictor of operative risk, even when the model was adjusted for sex.¹³

Most patients in our study received arterial grafts and among women their use was especially higher 78% compared with 64.8% reported in a recent study.³⁷ The lower fre-

quency of arterial grafting among women remains unexplained.^{15, 37} In our study the lower frequency of internal mammary artery grafting in women was partly the result of the higher proportion of women with diabetes mellitus. In addition other factors such as the smaller size and inadequate flow through the internal mammary artery in some patients may also be important. Internal mammary arterial grafts had more favourable intermediate and long-term patency rates than venous grafts.³⁸⁻⁴¹ In addition, grafting of the internal mammary artery reduced late cardiac events and increased long-term survival.³⁸

The analysis of predictors of mortality was limited because the univariate analysis lacked statistical power owing to the low number of deaths. Similarly, multivariate analysis could not be used because of the small number of events. Data on functional class, ventricular ejection fraction, and surgical technique (such as pump and ischaemic time) for women and men were not analysed in this study which focused on coronary risk factors.

In conclusion, risk factors for coronary artery disease were significantly more common in women undergoing CABG than in men. There was a slight but not statistically significant increase in hospital mortality in women compared with men. Preoperative diabetes mellitus seemed to be a significant predictor of in hospital mortality after CABG.

Further studies are needed to confirm our findings and establish their effect on mortality and the effect of risk factor modification on outcome. We hope that such studies will improve the application and results of CABG in women.

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